

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 15 JUN 2005

WFO PCT

To:

see form PCT/ISA/220

21/7

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

		Date of mailing (day/month/year) see form PCT/ISA/210 (second sheet)
Applicant's or agent's file reference see form PCT/ISA/220		FOR FURTHER ACTION See paragraph 2 below
International application No. PCT/US2004/042556	International filing date (day/month/year) 17.12.2004	Priority date (day/month/year) 29.12.2003
International Patent Classification (IPC) or both national classification and IPC C07D471/04, A61K31/437, A61P37/02		
Applicant 3M INNOVATIVE PROPERTIES COMPANY		

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/042556

Box No. I Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 a sequence listing
 table(s) related to the sequence listing
 - b. format of material:
 in written format
 in computer readable form
 - c. time of filing/furnishing:
 contained in the international application as filed.
 filed together with the international application in computer readable form.
 furnished subsequently to this Authority for the purposes of search.
3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/042556

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application,
 claims Nos. 14-16

because:

- the said international application, or the said claims Nos. (with respect to industrial applicability) relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet
- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the whole application or for said claims Nos.
- the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

- the written form has not been furnished
 does not comply with the standard
- the computer readable form has not been furnished
 does not comply with the standard
- the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/042556

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes:	Claims	1-18
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-18
Industrial applicability (IA)	Yes:	Claims	1-13,17,18
	No:	Claims	

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2004/042556

Reference is made to the following documents:

D1: US 2003/212092

D2: WERMUTH ET AL: "The Practise of Medicinal Chemistry" PRACTICE OF MEDICINAL CHEMISTRY, 1996, pages 203-237

Re Item III

Claims 14-16 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

- 1) The subject-matter of present claims 1-18 is new (Article 33(2) PCT).

The document D1 discloses immunomodulators of formula (I) (cf. claim 1 and examples 2, 3, 7-10, 23, 108, 115, 116, 118, 120, 122, 123, 146, 147 and 149).

The subject-matter of the present claims 1, 2, 17 and 18 differs from the compounds of D1 in that the substituent on the ring nitrogen atom does not comprise an oxygen atom in the linker X'-Z. Therefore, the claims are novel.

The dependent claims and the claims relating to the use of the new compounds are novel by consequence (Claims 3-12 and 14-16).

The claim 13, relating to a composition comprising the novel compounds, is also novel.

- 2) The subject-matter of claims 1-18 does not involve an inventive step (Article 33(3) PCT).

The document D1 represents the closes prior art (cf. above).

The technical problem underlying the present claims 1 and 2 is seen in the provision of alternative immunomodulators.

The problem appears to be solved by the replacement of the oxygen atom in the residue X-O-R₁ of D1 by a CH₂ group (cf. claim 1 and examples 2, 3, 7-10, 23, 108, 115, 116, 118, 120, 122, 123, 146, 147 and 149 of D1).

However, such an isosteric replacement does not involve an inventive step when the modified compounds only exhibit the same activity as the current compounds (see D2, page 209).

The present claims would only involve an inventive step if the claimed compounds showed unexpected properties or effects compared to the above mentioned compounds of D1.

The claims relating to a pharmaceutical composition, the claims relating to the use of the compounds and the claims relating to synthetic precursors of the compounds according to claim 1 and 2 would only involve an inventive step if the claims 1 and 2 fulfilled this requirement.

Remark

The term "non-interfering substituent" used in claim 1 does not satisfy the requirements of Article 6 PCT.

The term is to be seen as a functional feature. Functional features are, however, allowable only if the result is one which can be directly and positively verified by tests or procedures adequately specified in the description or known to a person skilled in the art and which do not require undue experimentation (cf. Guidelines, II, 5.35).